REMARKS/ARGUMENTS

The Pending Claims

Claims 5, 8, 10-12, 18, 20, and 32-35 are pending and are directed to a method of enhancing an immune response in a subject (claims 5, 8, 10-12, 32, and 34) and a method of treating a subject with a condition comprising a deficiency of at least one of memory B cells and plasma cells (claims 18, 20, 33, and 35). Claim 8 has been withdrawn by the Office as directed to non-elected subject matter.

Amendments to the Specification

The specification has been amended to include a replacement sequence listing comprising SEQ ID NO: 17 and include an incorporation-by-reference of electronically filed material (i.e., the replacement sequence listing).

Additionally, the specification has been amended to include a sequence identification number (i.e., SEQ ID NO: 17) following WSXWS at page 19, line 20.

No new matter has been added by way of these amendments to the specification.

Amendments to the Claims

The claims have been amended to point out more particularly and claim more distinctly the invention. In particular, claim 5 has been amended to incorporate the features of claims 7 and 9. Accordingly, claims 7 and 9 have been canceled. Claim 5 has also been amended to recite that the IL-21 polypeptide comprises the amino acid sequence of SEQ ID NO: 1 and that the IL-21 agonists retain the activity of the IL-21 polypeptide as supported by the specification at, for example, page 7, line 10, and page 8, lines 6-13. Claims 10 and 12 have been amended to depend from claim 5.

Claim 18 has been rewritten as independent claim. Claim 19 has been canceled. Claim 20 has been amended to depend from claim 18.

Claims 6, 13-17 and 21-31 have been canceled as directed to non-elected subject matter.

Claims 32-35 are new and are supported by the specification at, for example, page 7, line 10; page 8, lines 6-13; and page 31, lines 14-27.

No new matter has been added by way of these amendments.

Summary of the Office Action

The Office makes final the restriction requirement and withdraws claims 6, 8, 13-17, and 21-31 from consideration.

The Office objects to the specification for allegedly containing a sequence without a sequence identifier.

The Office rejects claims 5, 7, 9-12, and 18-20 under 35 U.S.C. § 112, first paragraph, for allegedly lacking written description and enablement.

Reconsideration of these objections and rejections is hereby requested.

Discussion of Claim 8

The Office has withdrawn claim 8 from consideration as allegedly drawn to subject matter of a non-elected group (Group II). However, Applicants believe that claim 8 could be a member of elected Group I, as well as non-elected Group II. In particular, Applicants note that claim 20, which is directed to similar subject matter as claim 8, was assigned to both Groups I and II. Therefore, Applicants ask that claim 8 be rejoined and examined with the elected claims of Group I.

Discussion of the Objection to the Specification

The Office objects to the specification for not providing a sequence identifier for the sequence at page 19, line 20. Applicants have amended the specification to insert a sequence identifier (i.e., SEQ ID NO: 17) for this sequence and included a replacement sequence listing with SEQ ID NO: 17. Therefore, Applicants request that the objection to the specification be withdrawn.

Discussion of the Section 112, First Paragraph, Rejections

The Office contends that the specification does not provide adequate written description or enablement for the genus of IL-21 or unspecified IL-21 agonists thereof because the genus is highly variable.

The pending claims, as amended, recite an IL-21 polypeptide comprising the amino acid sequence of SEQ ID NO: 1 (i.e., human IL-21 polypeptide) or an agonist thereof, wherein the agonist retains the ability to bind to the IL-21 receptor and produce the same physiological effect produced by binding of the IL-21 polypeptide comprising the amino acid sequence of SEQ ID NO: 1 to the IL-21 receptor.

Therefore, the claims require that the IL-21 agonist binds to the IL-21 receptor. Assays to determine receptor binding are known in the art. Additionally, the claims require that the IL-21 agonist produce the same physiological effect produced by binding of the IL-21 polypeptide to the IL-21 receptor. The specification describes that the IL-21 polypeptide activates the JAK/STAT signaling pathway (see, e.g., page 8, line 30, through page 9, line 5), induces differentiation of B cells and B cell progenitors into memory B cells and/or plasma cells (see, e.g., page 9, lines 6-20), induces expression of mRNA for Blimp-1 and Bcl-6 (see, e.g., page 53, lines 27-29), and inhibits expression of Pax5 mRNA (see, e.g., page 53, lines 27-30). Assays to determine if an IL-21 agonist produces the above-described effects (e.g., real-time PCR) are known in the art and are described in the specification at, for instance, page 41, line 19, through page 44, line 16; and Examples 3-5.

Accordingly, based on the teachings in the specification and what was known in the art, one of ordinary skill in the art would have recognized what was meant by a IL-21 agonist, as well as methods to identify a IL-21 agonist for use in the inventive methods.

The Office also contends that the specification is not enabling for ex vivo methods of therapy. In particular, the Office contends that the specification does not provide any examples of ex vivo therapy or therapy against a viral antigen. The Office contends that memory B cells and plasma cells neutralize extracellular pathogens, but that a viral antigen is considered to be an intracellular antigen, such that antibody generation would require co-exposure of the B cell population to a viral antigen.

Applicants note that there is no requirement for working examples in the specification for an enabling specification. The specification discloses that a population of cells (e.g., B cell progenitors) that have been isolated from a subject can be contacted with IL-21 polypeptide or an IL-21 agonist, which results in the differentiation of the B cells into plasma cells and/or memory cells, which are then isolated (see, e.g., page 34, line 18, through page 35, line 3; and Examples 3-5). Furthermore, the specification discloses the administration of the isolated memory B cells and plasma cells to the subject to enhance an immune response (see, e.g., page 34, line 18, through page 35, line 3). Since antibody production (e.g., by plasma cells) is an essential element of the immune response, one of ordinary skill in the art would recognize that the inventive methods would be effective in enhancing an immune response in a subject.

With regard to the Office's contention that viral antigens are intracellular, Applicants note that claims 5 and 18 (and, thus, claims dependent, thereon) recite that the method optionally comprises the administration of an antigen to the B cell population. Accordingly, the claims encompass the administration of an antigen, such as a viral antigen, to the B cell population. Applicants also note that viruses can be extracellular early in the course of infection in the case of viruses that produce latent infections (i.e., viruses that reside in host cells and produce proteins that may alter cellular functions) or during infection in the case of viruses that produce lytic infections (i.e., viruses that cause a host cell to lyse releasing viral particles into the extracellular space). Therefore, viral antigens can be extracellular antigens against which an immune response in the form of antibodies (e.g., against antigens of the viral envelope) would be therapeutic. For example, in HIV infection, the immune system generates antibodies against HIV envelope proteins, gp120 and gp41.

Accordingly, based on the teachings in the specification and what was known in the art, one of ordinary skill in the art would have recognized how to perform the inventive methods to enhance an immune response and treat a subject in need without undue experimentation and with an expectation of success.

The Office contends that the claims encompass the administration of heterologous (e.g., allogeneic and xenogeneic) populations of B cells to the subject, including B cells from dolphins or squirrels into a human. The pending claims recite that the population of B cells is

isolated from a subject, treated, and then introduced into the subject. Therefore, the B cells are not from different species or different humans.

For the above described reasons, the pending claims are adequately described and enabled by the specification and the Section 112, first paragraph, rejections should be withdrawn.

Conclusion

Applicants respectfully submit that the patent application is in condition for allowance. If, in the opinion of the Examiner, a telephone conference would expedite the prosecution of the subject application, the Examiner is invited to call the undersigned attorney.

Respectfully submitted,

Jeremy M. Jay, Reg. No. 35,587
LEYDIG, VOIT & MAYER
700 Thirteenth Street, N.W., Suite 300
Washington, DC 20005-3960
(202) 737-6770 (telephone)
(202) 737-6776 (facsimile)

Date: 17 Jan. 2008

Notice to Comply	Application No. 10/579,988	Applicant(s) LEONARD ET AL.	
	Examiner Maria Leavitt	Art Unit 1633	

NOTICE TO COMPLY WITH REQUIREMENTS FOR PATENT APPLICATIONS CONTAINING NUCLEOTIDE SEQUENCE AND/OR AMINO ACID SEQUENCE DISCLOSURES

Applicant must file the items indicated below within the time period set the Office action to which the Notice is attached to avoid abandonment under 35 U.S.C. § 133 (extensions of time may be obtained under the provisions of 37 CFR 1.136(a)).

The nucleotide and/or amino acid sequence disclosure contained in this application does not comply with the requirements for such a disclosure as set forth in 37 C.F.R. 1.821 - 1.825 for the following reason(s):

☒ 1. This application clearly fails to comply with the requirements of 37 C.F.R. 1.821-1.825. Applicant's attention is directed to the final rulemaking notice published at 55 FR 18230 (May 1, 1990), and 1114 OG 29 (May 15, 1990). If the effective filing date is on or after July 1, 1998, see the final rulemaking notice published at 63 FR 29620 (June 1, 1998) and 1211 OG 82 (June 23, 1998).

☐ 2. This application does not contain, as a separate part of the disclosure on paper copy, a "Sequence Listing" as required by 37 C.F.R. 1.821(c).

☐ 3. A copy of the "Sequence Listing" in computer readable form has not been submitted as required by 37 C.F.R. 1.821(e).

☐ 4. A copy of the "Sequence Listing" in computer readable form has been submitted. However, the content of the computer readable form does not comply with the requirements of 37 C.F.R. 1.822 and/or 1.823, as indicated on the attached copy of the marked -up "Raw Sequence Listing."

☐ 5. The computer readable form that has been filed with this application has been found to be damaged and/or unreadable as indicated on the attached CRF Diskette Problem Report. A Substitute computer readable form must be submitted as required by 37 C.F.R. 1.825(d).

☐ 6. The paper copy of the "Sequence Listing" is not the same as the computer readable from of the "Sequence Listing" as required by 37 C.F.R. 1.821(e). The correct SEQ ID NO:2 is present in the paper copy of the of the sequence listing only. Therefore a search of the correct sequence is not possible.

☒ 7. Other: In this instance, at page 19, line 20 of the specification discloses the following amino acid sequence, "WSXWS" that is not identified by sequence identification number. Furthermore, this sequence does not appear in the sequence listing as filed.

Applicant is required to submit:

☒ An initial or substitute computer readable form (CRF) copy of the "Sequence Listing".

☒ An initial or substitute paper copy of the "Sequence Listing", **as well as an amendment specifically directing its entry into the application**.

☒ A statement that the content of the paper and computer readable copies are the same and, where applicable, include no new matter, as required by 37 C.F.R. 1.821(e) or 1.821(f) or 1.821(g) or 1.825(b) or 1.825(d).

For questions regarding compliance to these requirements, please contact:

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